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TOPICAL HAZARD EVALUATION OF CANDIDATE INSECT REPELLENT AI3-357--ETC(U)
NOV 76 K C SWENTZEL, D L BUMGARDNER

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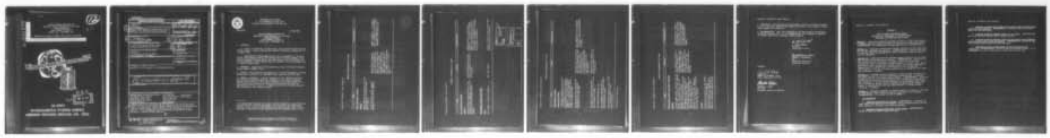

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TOPICAL HAZARD EVALUATION OF CANDIDATE INSECT REPELLENT AI3-35716-aGb N-HEXYLVALERAMIDE

STUDY NUMBER 51-0804-77

AUGUST 1975 - SEPTEMBER 1976

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Sprague-Dawley Wistar-derived rats	AI3-35716-aGb	photochemical
New Zealand White rabbits	skin sensitization	guinea pigs
approximate lethal dose	insect repellent	
Topical Hazard Evaluation	skin irritation	
N-Hexylvaleramide	eye irritation	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A hazard evaluation of AI3-35716-aGb was conducted using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. It was recommended that AI3-35716-aGb be approved for further testing as a candidate insect repellent.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT/WP

4 NOV 1976

TOPICAL HAZARD EVALUATION OF
CANDIDATE INSECT REPELLENT AI3-35716-aGb
N-HEXYLVALERAMIDE
STUDY NUMBER 51-0804-77
AUGUST 1975 - SEPTEMBER 1976

1. AUTHORITY.

a. Letter, US Department of Agriculture, Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, FL, 14 August 1975.

b. Memorandum of Understanding Between the US Department of the Army, Office of The Surgeon General, The US Army Health Services Command, The US Army Environmental Hygiene Agency, the Armed Forces Pest Control Board and the US Department of Agriculture, effective December 1970 with Amendment No. 1, effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-35716-aGb.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-35716-aGb N-hexylvaleramide was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*

* The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," as prepared by the Committee on Revision of the "Guide for Laboratory Animal Facilities and Care," of the Institute of Laboratory Animal Resources, National Research Council (1972)

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Study No. 51-0804-77, Aug 75-Sep 76

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Skin Irritation Studies		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.		
0.5 ml technical grade compound applied to each of six rabbits.	AI3-35716-aGb produced very slight erythema in one of six rabbits in 24 hours at the intact skin site and very slight erythema in three of six rabbits as well as very slight edema in one of six rabbits at the abraded skin sites in 24 and 72 hours.	USAEHA Category I (ref Appendix). There is no restriction for acute application of this compound to the human skin.

Study No. 51-0804-77, Aug 75-Sep 76

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Eye Irritation Studies		
Rabbits		
Single 24-hour application of 0.1 ml technical grade compound to one eye of of each of six New Zealand White rabbits.	AI3-35716-aGb did not produce an irritation reaction in the eyes.	USAEHA Category A (Reference Appendix). Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.
Approximate Lethal Dose (ALD)		
Oral		
Rats (male) - corn oil diluent.	ALD >4311 mg/kg	Presents little lethal hazard from acute accidental ingestion.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Sensitization Studies		
Guinea Pigs (Male)		
Intradermal injections of 0.1 ml of a 0.1 percent solution (w/v) of AI3-35716-aGb or of a 0.1 percent suspension of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of normal saline.		
Ten test guinea pigs received and challenged with a 0.1 percent solution of AI3-35716-aGb.	Challenge dose of AI3-35716-aGb (last intradermal injection) produced a slight irritation reaction in 1 of 10 guinea pigs, however, an irritation reaction was also observed in 2 of 5 cage controls.	Test compound did not sensitize guinea pigs and is not expected to cause a sensitization reaction in humans.
Ten positive control guinea pigs received and challenged with 0.1 percent suspension of DNCB.	Positive control (DNCB) produced sensitization in 10 of 10 guinea pigs.	
Ten cage control guinea pigs		
Five receiving challenge dose of AI3-35716-aGb at 0.1 percent without prior sensitizing doses.		
Five receiving challenge dose of DNCB at 0.1 percent without prior sensitizing doses.		

* A known skin sensitizer.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Photochemical Skin Irritation Studies		
Rabbits A single application (0.05 ml) of a 25 percent (w/v) solution of the compound and of a 10 percent (w/v) oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six New Zealand White rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10 to 15 cm. Application area was checked for irritation at 24, 48, and 72 hours.	UV irradiation caused an overall increase of erythema and edema after application of AI3-35716-aGb, however, this increase was not sufficient to classify this compound as a photochemical irritant.	Compound did not cause a a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation reaction in humans.
Control Following UV exposure of the rabbits, 0.05 ml of the test compound, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites.		

5. CONCLUSION. AI3-35716-aGb did not produce a positive irritation reaction in any of the tests conducted and should not present a toxic hazard to humans under proposed use conditions.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (reference paragraph 1b), it is recommended that AI3-35716-aGb be approved for further testing as a candidate insect repellent.

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APPENDIX

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATETORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.